REMARKS

The Invention

The present invention relates to recombinant nucleic acid molecules that encode fusion polypeptides. The recombinant nucleic acid molecules comprise a Ral2 polynucleotide sequence and a heterologous polynucleotide sequence. The Ral2 polynucleotide sequence consists of the sequence set forth in SEQ ID NO:3.

Status of the Claims

Claims 1-16, 27-29, and 31 are pending. Claims 7-9,12, 17-26 and 30 have been canceled without prejudice to future prosecution. Applicants have amended claims 1, 10, 11, 13, and 27 and respectfully request entry of these amendments. As amended, claims 1 and 27 recite "wherein the Ral2 polynucleotide sequence consists of the sequence set forth in SEQ ID NO:3." Support for these amendments can be found throughout the specification and claims as originally filed, (*see, e.g.*, specification at page 2, lines 24-26; page 6, lines 7-8; and claim 12). Claims 10, 11, and 13 have been amended solely to ensure correct claim dependency. Thus, no new matter has been introduced by these amendments.

A version of the claims with markings to show changes to the claims is provided in Appendix A. All of the pending claims are provided in Appendix B for the Examiner's convenience.

In the Office Action mailed August 26, 2002, the pending claims were rejected, in various combinations, under 35 U.S.C. § 112, first paragraph; under 35 U.S.C. § 112, second paragraph; under 35 U.S.C. § 102(e); and under 35 U.S.C. § 103. Each of these rejections is addressed below.

Objection to the drawings

The Office Action states that the drawings are acceptable subject to correction of informalities. A set of formal drawings is submitted concurrently with this Amendment and Response. Therefore, Applicants respectfully request withdrawal of this objection.

Objection to the specification

The specification has been objected to for alleged informalities. Each of the informalities is addressed in turn below, in the order raised by the Examiner.

1. Page 2, line 21

The specification at page 2, line 21 has been objected to for the recitation of the acronyms "DPPD" and "WT1." In accordance with the Examiner's suggestion, the specification at page 2, line 21 has been amended to recite "D Purified Protein Derivative ("DPPD")" and "Wilm's Tumor Gene ("WT1")". Therefore, Applicants respectfully request withdrawal of this objection.

2. Page 12, line 31

The specification at page 12, line 31 has been objected to for the recitation of the acronyms "CaMV" and "TMV." In accordance with the Examiner's suggestion, the specification at page 12, line 31 has been amended to recite "cauliflower mosaic virus ("CaMV") and "tobacco mosaic virus ("TMV")." Therefore, Applicants respectfully request withdrawal of this objection.

3. Page 20, line 12

The specification at page 20, line 12 has been objected to for the recitation of the abbreviation "polyHis." In accordance with the Examiner's suggestion, the specification at page 20, line 12 has been amended to recite "poly Histidine ("polyHis")." Therefore, Applicants respectfully request withdrawal of this objection.

4. Pages 4-5

The specification at the paragraph bridging pages 4-5 has been objected to for the phrase "the term 'Ral2 polypeptide' or 'Ral2 polynucleotide' as used herein refer to the native Ral2 sequences (*e.g.*, SEQ ID NO:3 or SEQ ID NO:4)" because SEQ ID NO:4 refers to a polypeptide and SEQ ID NO:3 refers to a polynucleotide. In accordance with the Examiner's suggestion, the specification starting at page 4, line 34 has been amended to recite ""the term 'Ral2 polypeptide' or 'Ral2 polynucleotide' as used herein refer to the native Ral2 sequences (*e.g.*, SEQ ID NO:4 or SEQ ID NO:3, respectively)." Accordingly, Applicants respectfully request withdrawal of this objection.

5. Page 6, line 31 and 32

The specification at page 6, line 31 has been objected to for the phrase "at least about 25 to about 50 amino acids or nucleotides" and the specification at page 6, lines 31-32 has been objected to for the phrase "75-100 amino acids or nucleotides." In accordance with the Examiner's suggestion, the specification starting at page 6, line 31 has been amended to recite "at least about 25 to about 50 nucleotides in length, at least about 75-100 nucleotides in length, or a nucleotide sequence encoding at least about 25 to about 50 amino acids, or a nucleotide sequence encoding at least about 75- 100 amino acids." Therefore, Applicants respectfully request withdrawal of this objection.

6. Page 9, lines 3 and 4

The specification at page 9, line 3 has been objected to for the phrase "a defined ionic strength pH" and page 9, line 4 has been objected to for the phrase "and nucleic concentration." In accordance with the Examiner's suggestion, the specification at page 9, line 3 has been amended to recite "a defined ionic strength and pH" and the specification at page 9, line 4 has been amended to recite "nucleic acid concentration." Therefore, Applicants respectfully request withdrawal of this objection.

7. Page 13, line 16

The specification at page 13, line 16 has been objected to for the phrase "mammalian cell systems." Applicants respectfully assert that those of skill in the art appreciate that the cell lines listed after the phrase "mammalian cell systems" are one component of a mammalian cell based recombinant protein expression system. Accordingly, the specification at page 13, line 16 has been amended to recite "mammalian cell systems (*e.g.*, COS, CHO, BHK, 293, 3T3 cells transformed with suitable expression vectors)." Therefore, Applicants respectfully request withdrawal of this objection.

8. Page 16, lines 28-29

The specification at page 16, lines 28-29 has been objected to for the phrase "Ra12 polynucleotide sequences (*e.g.*, SEQ ID NO:4)." In accordance with the Examiner's suggestion, the specification at page 16, lines 28-29 has been amended to recite "Ra12 polynucleotide sequences (*e.g.*, SEQ ID NO:3)." Therefore, Applicants respectfully request withdrawal of this objection.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-16, 27-29, and 31 are rejected under 35 U.S.C. §112, first paragraph as allegedly nonenabled for all polynucleotide variants of the polynucleotide sequence set forth in SEQ ID NO:3. In making the rejection, the Examiner acknowledges that the specification is enabling for a Ra12 polynucleotide sequence of SEQ ID NO:3. Claim 1 has been amended to recite an "Ra12 polynucleotide sequence [that] is the sequence set forth in SEQ ID NO:3."

In view of the foregoing, Applicants respectfully submit that the claims are fully enabled. Accordingly, Applicants urge the Examiner to withdraw the rejection under 35 U.S.C. § 112, first paragraph.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-16, 27-29, and 31 are rejected under 35 U.S.C. §112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

As set forth in MPEP § 2173.02, "[d]efiniteness of claim language, must be analyzed in light of (A) content of the application; (B) the teachings of the prior art; and (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

In the instant case, the specification adequately defines the terms or the terms are adequately understood to one of skill in the art, such that the claims are not indefinite under 35 U.S.C. §112, second paragraph. Several bases of indefiniteness were raised, and they will be discussed in turn.

1. Claim 1

Claim 1 has been rejected because the recitation "wherein the Ra12 polynucleotide sequence hybridizes to SEQ ID NO:3 under stringent conditions" is allegedly unclear. Claim 1 has been amended to recite "wherein the Ra12 polynucleotide sequence consists of the sequence set forth in SEQ ID NO:3." Accordingly, Applicants respectfully request withdrawal of this rejection.

2. Claims 7-9

Claims 7-9 have been rejected as allegedly unclear. Claims 7-9 have been canceled. Accordingly, Applicants respectfully request withdrawal of this rejection as moot.

3. Claim 27

Claim 27 has been rejected because the recitation "is encoded by a Ra12 polynucleotide sequence that hybridized to SEQ ID NO:3 under stringent conditions" is

allegedly unclear. Claim 27 has been amended to recite wherein the Ra12 polynucleotide sequence consists of the sequence set forth in SEQ ID NO:3." Accordingly, Applicants respectfully request withdrawal of this rejection.

4. Claim 29

Claim 29 has been rejected as allegedly unclear for omitting essential steps, *i.e.*, omitting the steps of screening recombinant clones and selecting positive clones. Claim 29 is dependent on claim 27 and is directed to a method of producing a fusion polypeptide by expressing in a host cell a recombinant nucleic acid molecule that encodes a fusion polypeptide and purifying the fusion polypeptide from the host cell. Claim 29 is directed to a method of ***producing*** a fusion polypeptide, not to methods of screening recombinant clones that express the fusion polypeptide. One of skill in the art would appreciate that screening recombinant clones is not required to produce fusion polypeptides. Thus, Applicants respectfully submit that the claims are definite. Accordingly, Applicants urge the Examiner to withdraw the rejection under 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. § 102(e)

Claims 1, 3, 7-9, 12-16, 27, 29, and 31 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Reed *et al.* (U.S. Patent No. 6,350,456).

For a rejection of claims under § 102(e) to be properly founded, the Examiner must establish that a single prior art reference discloses each and every element of the claimed invention. *See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). In *Scripps Clinic & Research Found. v. Genentech, Inc.*, 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991), the Federal Circuit held:

> [A]nticipation requires that all of the elements and limitations of the claim are found with a single prior art reference. . . .There must be ***no difference***

> between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention.

Id. at 1010 (emphasis added). Anticipation can be found, therefore, only when a cited reference discloses ***all*** of the elements, features or limitations of the presently claimed invention.

As explained above, the present invention relates to recombinant nucleic acid molecules that encode fusion polypeptides. The recombinant nucleic acid molecules comprise a Ral2 polynucleotide sequence and a heterologous polynucleotide sequence. The claims have been amended to recite that the Ral2 polynucleotide sequence consists of the sequence set forth in SEQ ID NO:3, a 396 base nucleic acid sequence.

Reed *et al.* was the first to disclose a genus of polynucleotide sequences and the corresponding amino acid sequences for a genus of fusion proteins comprising Ral2. In particular, Reed *et al.* disclose a 447 base polynucleotide sequence for Ral2 (SEQ ID NO:4 of Reed *et al.*). In contrast to Reed *et al.*, the present invention is directed to a previously undisclosed variant of the polynucleotide sequence encoding an Ral2 polypeptide, *i.e.*, SEQ ID NO:3, a 396 base polynucleotide sequence. SEQ ID NO:4 of Reed *et al.* is not the same sequence as SEQ ID NO:3 as disclosed and claimed in the present application. Applicants respectfully submit that SEQ ID NO:3 is a separately patentable species of the Ral2 polynucleotide genus disclosed in Reed *et al.* Therefore, Reed *et al.* does not disclose all of the elements of the claimed recombinant nucleic acid molecules that encode fusion polypeptides, wherein the Ral2 polynucleotide sequence consists of the separately patentable sequence set forth in SEQ ID NO:3, and does not anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §102(e) be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Claims 1, 3, 7-9, 12-16, 27, 29, and 31 are rejected under 35 U.S.C. § 103 as allegedly obvious over Reed *et al.*, taken with Madsen *et al.* (U.S. Patent No.

6,133,023) and Burrows *et al.* (U.S. Patent No. 6,270,772). Applicants respectfully traverse.

> As set forth in M.P.E.P. § 2143, "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. *First*, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *Second*, there must be a reasonable expectation of success. *Finally*, the prior art reference (or references when combined) must teach or suggest all the claim elements. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

The present invention relates to recombinant nucleic acid molecules that encode fusion polypeptides. The recombinant nucleic acid molecules comprise a Ral2 polynucleotide sequence and a heterologous polynucleotide sequence. The claims, as amended, recite that the Ral2 polynucleotide sequence consisting of the sequence set forth in SEQ ID NO:3, a 396 base polynucleotide sequence.

As discussed above, Reed *et al.* does not disclose all of the elements, features or limitations of the presently claimed invention, *i.e.*, Reed *et al.* discloses a genus of polynucleotides and corresponding amino acid sequences for a genus of fusion proteins comprising Ral2. The sequences disclosed by Reed *et al.* are not the same as SEQ ID NO:3, a previously undisclosed 396 base polynucleotide sequence that is a separately patentable species of Ral2. Likewise, neither Madsen *et al.* nor Burrows *et al.* teach or suggest a Ral2 polynucleotide sequence that consists of the sequence set forth in SEQ ID NO:3 of the instant application.

Madsen *et al.* is cited as teaching an expression vector for a fusion protein wherein a portion of the fusion polypeptide is derived from *M. tuberculosis*, that the expression vector contains a cleavage site for peptidase, and an affinity tag. However, *none* of the sequences disclosed in Madsen *et al.* are a Ral2 polynucleotide sequence that

consists of the sequence set forth in SEQ ID NO:3 as disclosed and claimed in the present invention. Burrows *et al.* is cited as teaching that a peptide linker of an expression vector contains a cleavage site for a specific protease action. As acknowledged by the Examiner, Burrows *et al.* does not teach or suggest a Ral2 polynucleotide sequence that is the sequence set forth in SEQ ID NO:3 of the instant application. Thus, neither Madsen *et al.* nor Burrows *et al.*, alone or in combination, teach or suggest a Ral2 polynucleotide sequence that consists of the sequence set forth in SEQ ID NO:3 as disclosed and claimed in the present invention.

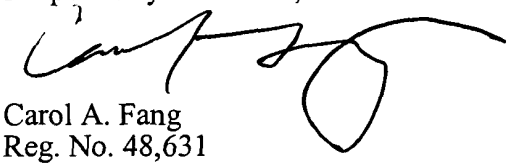
Therefore, even if the teachings of Reed *et al.*, Madsen *et al.*, and Burrows *et al.* were combined, the combination would not lead to the claimed invention because none of the cited references teach or suggest the claimed recombinant nucleic acid molecules that encode fusion polypeptides, wherein the Ral2 polynucleotide sequence consists of the sequence set forth in SEQ ID NO:3. Accordingly, Applicants respectfully request withdrawal of this rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,



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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Please insert the following replacement paragraph starting at page 2, line 9:

In one aspect, the present invention provides recombinant nucleic acid molecules that encode a fusion polypeptide, the recombinant nucleic acid molecules comprising a Ral2 polynucleotide sequence and a heterologous polynucleotide sequence, wherein the Ral2 polynucleotide sequence hybridizes to SEQ ID NO:3 under stringent conditions. In one embodiment, the recombinant nucleic acid molecules comprise a Ral2 polynucleotide sequence which is located 5' to a heterologous polynucleotide sequence. In another embodiment, the recombinant nucleic acid molecules further comprise a polynucleotide sequence that encodes a linker peptide between the Ral2 polynucleotide sequence and the heterologous polynucleotide sequence, wherein the linker peptide may comprise a cleavage site. In yet another embodiment, the recombinant nucleic acid molecules encode fusion polypeptides which further comprise an affinity tag. In yet another embodiment, the recombinant nucleic acid molecules encode a fusion polypeptide comprising a [DPPD, a WT1] D Purified Protein Derivative ("DPPD"), a "Wilm's Tumor Gene ("WT1"), a mammaglobin, or a H9-32A heterologous polypeptide. In yet another embodiment, the recombinant nucleic acid molecules comprise a Ral2 polynucleotide sequence comprising at least about 30 nucleotides, at least about 60 nucleotides, or at least about 100 nucleotides. In yet another embodiment, the recombinant nucleic acid molecules comprise a Ral2 polynucleotide sequence as shown in SEQ ID NO:3. In yet another embodiment, the recombinant nucleic acid molecules comprise a Ral2 polynucleotide sequence that encodes a Ral2 polynucleotide as shown in SEQ ID NO:4, SEQ ID NO:17 or SEQ ID NO:18.

Please insert the following replacement paragraph starting at page 4, line 29:

Surprisingly, it was discovered by the present inventors that a 14 KD C-terminal fragment of the MTB32A coding sequence expresses at high levels on its own and remains as a soluble protein throughout the purification process. This 14 KD C-terminal fragment of the MTB32A is referred herein as Ra12 (having amino acid residues 192 to 323 of MTB32A). The nucleic acid and amino acid sequences of native Ra12 are shown, *e.g.*, in Figures 2-6. As described in detail below, the term "Ra12 polypeptide" or "Ra12 polynucleotide" as used herein refer to the native Ra12 sequences [(*e.g.*, SEQ ID NO:3 or SEQ ID NO:4)] (*e.g.*, SEQ ID NO:4 or SEQ ID NO:3, respectively), their variants, or fragments thereof (e.g., SEQ ID NO:17 or SEQ ID NO:18). The present invention utilizes these properties of Ra12 polypeptides and provides recombinant nucleic acid molecules, expression vectors, host cells, and methods for stable and high yield expression of fusion polypeptides comprising a Ra12 polypeptide and a heterologous polypeptide of interest. The materials and methods of the present invention are particularly useful in expressing certain heterologous polypeptides (*e.g.*, DPPD) that other conventional expression methods failed to express in any substantial quantity.

Please insert the following replacement paragraph starting at page 6, line 22:

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide SEQ ID NO:3 or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide (SEQ ID NO:4) or a portion thereof. Optionally, the identity exists over a region that is at least about [25 to about 50 amino acids or nucleotides in length, or optionally over a region that is 75-100

amino acids or nucleotides in length] 25 to about 50 nucleotides in length, at least about 75-100 nucleotides in length, or a nucleotide sequence encoding at least about 25 to about 50 amino acids, or a nucleotide sequence encoding at least about 75- 100 amino acids."

Please insert the following replacement paragraph starting at page 8, line 29:

The phrase "stringent hybridization conditions" refers to conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acid, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found in Tijssen, *Techniques in Biochemistry and Molecular Biology--Hybridization with Nucleic Probes*, "Overview of principles of hybridization and the strategy of nucleic acid assays" (1993). Generally, stringent conditions are selected to be about 5-10 °C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength, pH, and nucleic acid concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m, 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (*e.g.*, 10 to 50 nucleotides) and at least about 60°C for long probes (*e.g.*, greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal is at least two times background, preferably 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42°C, or, 5x SSC, 1% SDS, incubating at 65°C, with a wash in 0.2x SSC, and 0.1% SDS at 65°C.

Please insert the following replacement paragraph starting at page 12, line 23:

Depending on the host/vector system utilized, any of a number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used in the expression vector. For example, when cloning in bacterial systems, inducible promoters such as pL of bacteriophage λ, plac, ptrp, ptac (ptrp-lac hybrid promoter; cytomegalovirus promoter) and the like may be used; when cloning in yeast cell systems, promoters such as ADHI, PGK, PHO5, or the α factor promoter may be used; when cloning in insect cell systems, promoters such as the baculovirus polyhedron promoter may be used; when cloning in plant cell systems, promoters derived from the genome of plant cells (*e.g.*, heat shock promoters; the promoter for the small subunit of RUBISCO; the promoter for the chlorophyll α/β binding protein) or from plant viruses (*e.g.*, the 35S RNA promoter of [CaMV] cauliflower mosaic virus ("CaMV"); the coat protein promoter of [TMV] tobacco mosaic virus ("TMV")) may be used; when cloning in mammalian cell systems, promoters derived from the genome of mammalian cells (*e.g.*, metallothionein promoter) or from mammalian viruses (*e.g.*, the adenovirus late promoter; the vaccinia virus 7.5K promoter) may be used; when generating cell lines that contain multiple copies of a the antigen coding sequence, SV40-, BPV- and EBV-based vectors may be used with an appropriate selectable marker.

Please insert the following replacement paragraph starting at page 13, line 6:

A variety of host-expression vector systems may be utilized to express a Ra12 fusion protein coding sequences. These include, but are not limited to, microorganisms such as bacteria (*e.g.*, *E. coli, B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing a coding sequence; yeast (*e.g.*, *Saccharomycdes, Pichia)* transformed with recombinant yeast expression vectors containing a coding sequence; insect cell systems infected with recombinant virus expression vectors (*e.g.*, baculovirus) containing a coding sequence; plant cell systems infected with recombinant virus expression vectors (*e.g.*, cauliflower

mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (*e.g.*, Ti plasmid) containing a coding sequence; or mammalian cell systems (*e.g.*, COS, CHO, BHK, 293, 3T3 cells transformed with suitable expression vectors). The expression elements of these systems vary in their strength and specificities.

The specification at page 13, line 16 has been objected to for the phrase "mammalian cell system." Therefore, Applicants respectfully request withdrawal of this objection.

Please insert the following replacement paragraph starting at page 16, line 27:

Thus, the terms such as "Ra12 polypeptide" or "Ra12 polypeptide sequence" as used herein refer to native Ra12 polynucleotide sequences [(*e.g.*, SEQ ID NO:4)] (*e.g.*, SEQ ID NO:3), fragments thereof (*e.g.*, SEQ ID NO:17 or 18), or any variants thereof. Functionally, a Ra12 polypeptide has the ability to produce a fusion protein, and its ability to produce a fusion proteins in host cells may be enhanced or unchanged, relative to the native Ra12 polypeptide (*e.g.*, SEQ ID NO:4), or may be diminished by less than 50%, and preferably less than 20%, relative to the native Ra12 polypeptide.

Please insert the following replacement paragraph starting at page 20, line 7:

One of skill would recognize that modifications can be made to the recombinant nucleic acids and fusion polypeptides without diminishing their biological activity. Some modifications may be made to facilitate the cloning, expression, or incorporation of the tag molecule into a fusion polypeptide. Such modifications are well known to those of skill in the art and include, for example, a methionine added at the amino terminus to provide an initiation site, or additional amino acids [(*e.g.*, poly His)] (*e.g.*, polyHistidine ("poly His")) placed on either terminus to create conveniently located restriction sites or termination codons or purification sequences.

IN THE CLAIMS

1. (Once amended) A recombinant nucleic acid molecule that encodes a fusion polypeptide, the recombinant nucleic acid molecule comprising a Ral2 polynucleotide sequence and a heterologous polynucleotide sequence, wherein the Ral2 polynucleotide sequence [hybridizes to] consists of the sequence set forth in SEQ ID NO:3[under stringent conditions].

7-9. (Cancel)

10. (Once amended) [The] A recombinant nucleic acid molecule [according to claim 1] that encodes a fusion polypeptide, the recombinant nucleic acid molecule comprising a Ral2 polynucleotide sequence and a heterologous polynucleotide sequence, wherein the Ral2 polynucleotide sequence encodes a Ral2 polypeptide [as shown in] consisting of the sequence set forth in SEQ ID NO:17.

11. (Once amended) [The] A recombinant nucleic acid molecule [according to claim 1] that encodes a fusion polypeptide, the recombinant nucleic acid molecule comprising a Ral2 polynucleotide sequence and a heterologous polynucleotide sequence, wherein the Ral2 polynucleotide sequence encodes a Ral2 polypeptide [as shown in] consisting of the sequence set forth in SEQ ID NO:18.

12. (Cancel)

13. (Once amended) [The] A recombinant nucleic acid molecule [according to claim 1] that encodes a fusion polypeptide, the recombinant nucleic acid molecule comprising a Ral2 polynucleotide sequence and a heterologous polynucleotide sequence, wherein the Ral2 polynucleotide sequence encodes a Ral2 polypeptide [as shown in] consisting of the sequence set forth in SEQ ID NO:4.

17-26. (Withdrawn)

27. (Once amended)A method of producing a fusion polypeptide, the method comprising expressing in a host cell a recombinant nucleic acid molecule that encodes a fusion polypeptide, the fusion polypeptide comprising a Ra12 polypeptide and a heterologous polypeptide, wherein the Ra12 polypeptide is encoded by a Ra12 polynucleotide sequence that [hybridizes to] consists of the sequence set forth in SEQ ID NO:3 [under stringent conditions].

30. (Withdrawn)